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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/522,351	SIMON, BRUCE J.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *30 April 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *6-8 and 13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,9-12 and 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *1/26/05,5/11/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-14 are pending.

Election/Restrictions

Applicant's election with traverse of Group I, claims 1-5 and 9-14, collagen from claim 12, and growth factors from claim 14, in the reply filed on April 30, 2007, is acknowledged. The traversal is on the ground(s) that two references cited in the international search report, Kipishidze et al. and Nicholson et al., do not anticipate the claims. This is not found persuasive because, as discussed below, Baylink and George et al. anticipate the composition claims. Moreover, Naughton et al. in combination with Baylink and George et al. render obvious claims 1-5, 9-12, and 14, while Shipley et al. in view of Baylink and/or George et al. render obvious claims 1, 3, 9, 11, 12, and 14.

Additionally, separate searches would be required for both groups of claims since Group I requires that the media is administered to the site of a tissue defect while Group II requires that the media is administered to a tissue culture. Clearly different steps are required for both groups, thus presenting undue search burden. Moreover, Group I requires the treatment of a tissue defect while Group II requires the cell proliferation is enhanced. The treatment of a tissue defect does not necessarily require that cell proliferation is enhanced.

The requirement is still deemed proper and is therefore made FINAL.

Claims 6-8 and 13 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention and species, there being no allowable generic or linking claim.

Claims 1-5, 9-12, and 14 are examined on the merits to the extent they read on the elected subject matter and species.

Information Disclosure Statement

The information disclosure statement filed January 26, 2005, fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. Specifically, no copies were provided of WO 99/50391, Macias et al., Nindl et al., or Spadara. It has been placed in the application file, but the information referred to therein has not been considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5, 9-12, and 14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Regarding undue experimentation, *In re Wands*, 8 USPQ2d 1400, at 1404 (Fed. Cir. 1988) states:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of

> experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (Citations omitted).

The claims are very broad in that they encompass methods and compositions for treating any tissue defect in a human or other animal subject. Further still, the specification defines "tissue defect" broadly as "any condition involving tissue which is inadequate for physiological or cosmetic purposes (page 4, lines 3-5). Thus, the complex nature of the subject matter of this invention is greatly exacerbated by the breadth of the claims. Moreover, there is a clear absence of working examples, as none of the examples in the specification provide any data to demonstrate the effectiveness of the instant invention in treating any tissue defect. Examples 1 and 2 in the specification appear to be prophetic examples. Finally, one would need to perform a large quantity of experimentation to identify all tissue cultures exposed to an electromagnetic field which result in media which are effective in treating all tissue defects, of which there are many types with complex and different characteristics.

In view of the breadth of the claims and the lack of guidance provided by the specification, the skilled artisan would have required an undue amount of experimentation to make and/or use the claimed invention. Therefore, claims 1-5, 9-12, and 14 are not considered enabled by the instant specification.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 2 and 3 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 2 is indefinite since the recitation "said tissue" lacks antecedent basis. It is unclear whether "said tissue" is the "living tissue" recited in step (a) of claim 1.

Claim 3 is indefinite since the recitation "said electromagnetic field stimulus" lacks antecedent basis. Parent claim 1 does not recite "electromagnetic field stimulus," and instead recites "an electromagnetic field."

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 9, 11, and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by Baylink (US 5,195,940).

Baylink discloses that "...the production of growth factor can be increased in vivo by the exogenous stimulation of living tissue with magnetic fields" (column 1, lines 53-55). Baylink teaches stimulating the production of growth factor in living tissue by the application of a

magnetic field (abstract). The magnetic field may be applied with an electromagnet (column 6, lines 50-51), and thus Baylink teaches the application of electromagnetic fields for enhanced growth factor production. Baylink emphasizes that "it is to be understood that the method of the present invention is suitable for use in stimulating growth factor in a range of living tissue, including but not limited to **in vitro cell cultures**, animal subjects, or human subjects" (column 5, lines 28-32, emphasis added). Example 1 at column 13 of the Baylink patent teaches a tissue culture of human osteosarcoma cells grown in DMEM medium which is subjected to a magnetic field (specifically, column 13, lines 11-15). The culture media were collected after magnetic field exposure (column 13, lines 21-23) and have increased production of growth factor (column 13, lines 57-60). Note that the DMEM medium can be considered a "pharmaceutically-acceptable carrier."

Although the reference does not specifically teach that the composition is effective for the treatment of tissue defects in a human or other animal subject, the compositions are the same, thus the claimed function must be inherent to the reference composition. The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new. As pointed out in MPEP §2112, "the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable".

A holding of anticipation is clearly required.

Claims 9, 11, and 14 are rejected under 35 U.S.C. 102(a) and 35 U.S.C. 102(e) as being anticipated by George et al. (US 6,334,069).

George et al. discloses the use of an electromagnetic field of specified strength and duration "...to stimulate cellular growth and proliferation,...growth factor expression,...and reductions in cell doubling time" (column 9, lines 12-17). George et al. accomplishes this by the administration of pulsed electromagnetic energy to cells (column 10, lines 4-7).

Example 1 in column 18 of the George patent describes the treatment of a fibroblast tissue culture with pulsed electromagnetic energy. The whole culture can be considered a composition comprising medium produced by electromagnetic stimulation of a tissue culture. Further still, Dulbecco's modified Eagle's medium present in the whole culture can be considered a "pharmaceutically-acceptable carrier."

Although the reference does not specifically teach that the composition is effective for the treatment of tissue defects in a human or other animal subject, the compositions are the same, thus the claimed function must be inherent to the reference composition. The discovery of a previously unappreciated property of a prior art composition, or of a scientific explanation for the prior art's functioning, does not render the old composition patentably new. As pointed out in MPEP §2112, "the claiming of a new use, new function or unknown property which is inherently present in the prior art does not necessarily make the claim patentable".

A holding of anticipation is clearly required.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-5, 9-12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton et al. (US 6,372,494) in view of Baylink (US 5,195,940) and/or George et al. (US 6,334,069).

Naughton et al. discloses conditioned cell medium compositions which are conditioned using any eukaryotic cell type (abstract). A culture medium is incubated with cells in order to obtain a "conditioned cell medium" (column 1, lines 30-32). The culture medium may be conditioned by stromal cells preferably in a three dimensional tissue construct (column 4, lines 49-53), which can be further cultured with parenchymal cells (column 5, lines 4-8). The stromal cells that can be cultured can include endothelial cells (column 12, lines 46-49), as required by instant claims 2 and 10.

Additionally, "the cells can be cultured by any means known in the art" (column 19, line 62) and once the culture medium is conditioned so that the extracellular proteins such as growth factors have reached desirable levels in the media, the conditioned medium is pumped out of the culturing system and processed for use (column 20, lines 15-19). It is noted in Naughton et al. that "...the conditioned media provided by the present invention is also useful in the treatment of other types of tissue damage, e.g. traumatic or congenital, wherein the repair and/or regeneration of tissue defects or damage is desired since many of these growth factors are found in Applicants' conditioned cell media..." (column 22, lines 4-9). For instance, the conditioned medium of Naughton et al. may be used in the treatment of broken bones (column 22, lines 27-31). Therefore, limitations recited in claims 4, 5, and 14 (culture medium for treatment of bone tissue defects wherein broken bone is a defect associated with osteoporosis, spinal fixation

procedure, joint replacement procedure, bone fracture; growth factors present in culture medium) are taught by Naughton et al. In order for the conditioned medium to be used for the treatment of tissue defects, the conditioned medium must be delivered to the site of said tissue defects. Further still, the conditioned medium may be formulated with a pharmaceutically acceptable carrier (column 5, lines 17-19) and the conditioned medium may contain collagens (column 25, lines 48-52), thus the limitations recited in instant claims 11 and 12 are disclosed.

Naughton et al. differs for the claimed invention in that it does not expressly disclose that the tissue culture for preparing the conditioned medium is subjected to an electromagnetic field.

Baylink discloses that "...the production of growth factor can be increased in vivo by the exogenous stimulation of living tissue with magnetic fields" (column 1, lines 53-55). Baylink teaches stimulating the production of growth factor in living tissue by the application of a magnetic field (abstract). The magnetic field may be applied with an electromagnet (column 6, lines 50-51), and thus Baylink teaches the application of electromagnetic fields for enhanced growth factor production. Baylink emphasizes that "it is to be understood that the method of the present invention is suitable for use in stimulating growth factor in a range of living tissue, including but not limited to in vitro cell cultures, animal subjects, or human subjects" (column 5, lines 28-32).

George et al. discloses the use of an electromagnetic field of specified strength and duration "...to stimulate cellular growth and proliferation,...growth factor expression,...and reductions in cell doubling time" (column 9, lines 12-17). George et al. accomplishes this by the administration of pulsed electromagnetic energy to cells (column 10, lines 4-7).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have applied an electromagnetic field, such as a pulsed electromagnetic field, to the tissue culture during incubation and prior to the extraction of the conditioned medium when performing the Naughton invention. One of ordinary skill in the art would have been motivated to do this since the application of an electromagnetic field would have increased growth factor production, thus resulting in a conditioned medium with a higher concentration of growth factors. Increased growth factor concentration is desirable since growth factors found in the conditioned media of Naughton et al. are for the treatment of tissue damage, regulate growth and differentiation, and accelerate wound healing (column 22, lines 4-26). Moreover, higher growth factor concentration is sought after by Naughton patent since it points out that the conditioned medium "...may be further processed to concentrate or reduce one or more factors or components contained within the medium. For example, the conditioned medium may be enriched with a growth factor..." (column 5, lines 23-28).

A holding of obviousness is clearly required.

Claims 1, 3, 9, 11, 12, and 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shipley et al. (WO 93/04164) in view of Baylink and/or George et al.

Shipley et al. discloses a method to produce human keratinocyte-derived conditioned medium factors (kdCMF) wherein "...human epithelial cells are cultured in protein-free medium to obtain a conditioned medium and recovering the conditioned medium from the culture" (page 3, lines 30-35). Shipley et al. notes that "in its simplest form, the kdCMF of the invention is simply the conditioned medium harvested from such cultures" (page 5, lines 28-30). The

kdCMF is used to promote healing of surface wounds, ulcerations, and other hypoproliferative skin pathologies (page 4, lines 1-5), and the kdCMF is applied to surface wounds with various pharmaceutically-acceptable carriers, including collagen (page 10, lines 8-27, particularly line 25). Thus, limitations recited in instant claims 11 and 12 are taught by the reference. It is noted that the kdCMF comprises a mixture of growth factors which provides efficacious results when applied to a wound in terms of increasing the rate of wound healing (page 4, lines 17-20).

Shipley et al. differs for the claimed invention in that it does not expressly disclose that the tissue culture of kerotinocytes for preparing the conditioned medium (kdCMF) is subjected to an electromagnetic field.

Baylink discloses that "...the production of growth factor can be increased in vivo by the exogenous stimulation of living tissue with magnetic fields" (column 1, lines 53-55). Baylink teaches stimulating the production of growth factor in living tissue by the application of a magnetic field (abstract). The magnetic field may be applied with an electromagnet (column 6, lines 50-51), and thus Baylink teaches the application of electromagnetic fields for enhanced growth factor production. Baylink emphasizes that "it is to be understood that the method of the present invention is suitable for use in stimulating growth factor in a range of living tissue, including but not limited to in vitro cell cultures, animal subjects, or human subjects" (column 5, lines 28-32).

George et al. discloses the use of an electromagnetic field of specified strength and duration "...to stimulate cellular growth and proliferation,...growth factor expression,...and reductions in cell doubling time" (column 9, lines 12-17). George et al. accomplishes this by the administration of pulsed electromagnetic energy to cells (column 10, lines 4-7).

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have applied an electromagnetic field, such as a pulsed electromagnetic field, to the tissue culture during incubation and prior to the extraction of the conditioned medium when performing the Shipley invention. One of ordinary skill in the art would have been motivated to do this since the application of an electromagnetic field would have increased growth factor production, thus resulting in a conditioned medium with a higher concentration of growth factors. Increased growth factor concentration is desirable since growth factors found in the conditioned media of Shipley et al. are for the treatment of increasing the rate of wound healing (page 4, lines 17-20).

A holding of obviousness is clearly required.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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